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EXPEDITED PROCEDURE
Group Art Unit: 1638
Docket No.: ICON 3.3-002
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Klimyuk et al.

Application No.: 10/030,793 Confirmation No.: 4086

Filed: January 11, 2002 Art Unit: 1638

For: METHOD OF MAKING PLANT ARTIFICIAL CHROMOSOMES Examiner: A. D. Mehta

COMMUNICATION

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Enclosed herewith is a Declaration under 37 C.F.R. § 1.132, executed by Dr. Victor Klimyuk, a named co-inventor of the above-cited patent application. This Declaration is being submitted to support the arguments set forth in Applicants' Amendment under 37 C.F.R. 1.116, filed March 7, 2006.

In his declaration, Dr. Klimyuk addresses the rejections based on non-enablement and obviousness. As stated in paragraph 4, it is Dr. Klimyuk's opinion that a person of skill in this art would be able to practice the method of claim 19 by following the teachings of the specification to produce chromosome fragments in whole plants after irradiation, and would appreciate that subjecting the whole plants to irradiation would not render the method inoperable for its intended purpose. Regarding the obviousness rejection, it is

Dr. Klimyuk's opinion that the teachings of *Famelaer* differ from the claimed invention in at least two respects; they do not teach the introduction of exogenous nucleic acid into a protoplast or whole plant prior to irradiation, and they do not teach selection for artificial minichromosomes containing the exogenous nucleic acid, and that exhibit normal plant chromosomal activities. It is also his opinion, as stated in paragraph 5, that a person in this field would not have been motivated to produce the claimed invention on the basis of the three cited references for, among other reasons, *Famelaer* observed that the presence of donor chromosomal material in chromosome fragments of the recipient (hybrid) was both random and unstable. Thus, as stated by Dr. Klimyuk, these findings were too unpredictable to motivate a person skilled in the art to use *Famelaer* as a basis for a method for producing artificial chromosome fragments containing nucleic acid (exogenous to a donor plant), and that exhibit normal plant chromosomal activities. Applicants respectfully request reconsideration and withdrawal of the rejections.

If there are any questions regarding this communication, please contact the Applicants' attorney at (908) 654-5000.

If there are any additional charges in connection with this Communication, the Examiner is authorized to charge Deposit

Account 12-1095 therefore.

Dated: May 16, 2006

Respectfully submitted,

By Shawn P. Foley

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DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Dr. Victor Klimyuk, do declare as follows:

1. I am a named co-inventor of the U.S. Patent Application 10/030,793, entitled "Method of Making Plant Artificial Chromosomes." I hold a number of degrees including a Masters of Science from Kiev University, 1980, and a Ph.D. from the Institute of Cell Biology and Genetic Engineering, in Kiev, 1987. I am currently Director of Development at Icon Genetics, a position I have occupied after acquisition of our company by Bayer AG at the beginning of January 2006. Before the acquisition, I was the Chief Scientific Officer of Icon Genetics AG in Germany, a position I held since 2003. Before joining Icon Genetics in 1999 as Research Director of its Halle (Germany) Laboratory, I worked in several academic institutions including the Institute of Protein Research of Russian Academy of Sciences (1980-1982), Biological Research Centre of Hungarian Academy of Science (1989-1990) and Sainsbury Laboratory, John Innes Centre, Norwich, UK (1991-1999). I have over 20 years of research and management experience in the fields of plant molecular biology, plant genetics and biotechnology.

2. I have authored over 30 publications in the fields of plant biotechnology, molecular biology and plant genetics, the latest including: *Santi et al.*, (2006), "Protection conferred by recombinant *Yersinia pestis* antigens produced by a rapid and scalable plant expression system", Proc. Natl. Acad. Sci. U.S.A, 103:861-866; *Marillonnet et al.*, (2005), "Systemic *Agrobacterium tumefaciens*-mediated transfection of viral replicons for efficient transient expression in plants", *Nat Biotechnol.*, 23(6):718-723; *Gils et al.*, (2005) "High-yield production of authentic human growth hormone using a plant virus-based expression system", *Plant Biotechnol. J.*, 3:613-620; *Gleba et al.*, (2005), "Magnifection--a new platform for expressing recombinant vaccines in plants", *Vaccine,* 23(17-18):2042-2048; *Klimyuk et al.*, (2005) "Production of recombinant proteins in Plants", in *"Modern Biopharmaceuticals"*, Ed. *Knaeblein*, Wiley-VCH, chapter 6, pp. 893-917; and *Marillonnet et al.*, (2004), "In planta engineering of viral RNA replicons: efficient assembly by recombination of DNA modules delivered by Agrobacterium", *Proc Natl Acad Sci U S A,* 101:6852-6857. In addition to my publications, I have also presented numerous lectures on the topic of plant biotechnology as invited speaker on international conferences, and am an inventor on more than 20 patents and patent applications.

3. I have reviewed the United States Patent Office Communications mailed June 7, 2005 and November 22, 2005, and I am familiar with the positions taken by the Examiner, particularly those based on "enablement" and "obviousness". I will address each of these in turn.

4. The Examiner has maintained a rejection of claim 19 "for lack of enablement." (Office Communication, November 22, 2005). The Examiner has indicated that the specification would not enable a person to produce chromosome fragments in whole plants because the "specification does not show that a whole plant survives the radiation, such that it can still be crossed." (Office Action, p. 5, June 7, 2005). The Examiner believes that irradiation kills the plant rendering it inoperable for the purposes of this invention. However, page 9 of the specification details how to irradiate whole plants to induce chromosome fragmentation, followed by crossing with a normal plant, thus reviving the irradiated plant and producing a hybrid. These techniques are illustrated in the *Pandey* publication (*Pandey*, 1975, *Nature* 256:310-313), referenced on page 9. Thus, by following the teachings of the specification, which include *Pandey*, one of skill in this art would be able to practice the invention of claim 19,

which includes transforming a plant with exogenous nucleic acid, irradiating a whole plant followed by crossing with a non-irradiated plant to produce chromosome fragments, and then identifying a hybrid plant, or cells, or protoplasts containing those chromosome fragments in a straight-forward manner.

5. The Examiner has also maintained that claims 1, 2, 5-16, and 18-44 would have been "obvious" and "unpatentable" in light of three publications: *Famelaer et al.* (Theor. Appl. Genet., Vol. 79, pages 513-520, 1990), *Blume et al.* (Plant J., Vol. 12, pages 731-746, 1997), and *Adam et al.* (Plant J., Vol. 11, pages 1349-1358, 1997). The Examiner's view is that "the only difference between *Famelaer* and the claims is the presence of transgenic nucleic acid in the chromosomes of the protoplasts to be irradiated." (Office Communication November 22). The Examiner contends that it would have been "obvious" to a person familiar with this art to incorporate *Blume* 's methods of producing protoplasts from transgenic plants, and *Adam*'s use of YAC vectors, to arrive at the present invention. After review of these publications, I disagree.

Each of the scientific publications cited by the Examiner teaches how to introduce a trait of interest into a plant genome via different methods. *Famelaer* teaches fusion of irradiated protoplasts and non-irradiated protoplasts to create parasexual hybrid plants. *Famelaer* observed random transfer of donor chromosomal material to the parasexual hybrid. He found, however, that this material from the donor was generally unstable and/or non-inheritable. Specifically, *Famelaer* conceded that his method produced overwhelmingly sterile progeny, or progeny incapable of normal function. (*Famelaer* at 513). These results would not have led a person skilled in this field to believe or even reasonably expect that any exogenous nucleic acid (*e.g.*, that was introduced into the donor plant prior to irradiation and crossing) would have been transferred to the hybrid (*i.e.*, recipient) in a stable, inheritable fashion. Thus, there is not one, but at least two key differences between the cited scientific publications and the claimed invention. Namely, none of the publications teaches (1) the introduction of protoplasts or whole plants with exogenous nucleic acid prior to irradiation, or (2) selection for artificial minichromosomes containing the exogenous nucleic acid, and that exhibit normal plant chromosomal activities, as taught by my invention.

Blume and *Adam* teach how to introduce a trait of interest into a plant genome using specific instructs, via standard transformation techniques. *Blume* discloses inserting a GUS coding region into a restriction enzyme site in a plant transformation vector. *Adam* teaches

the use of YAC vectors to stably transform plant cells. These references teach no more than well-known transformation techniques, and vectors that may be useful in such techniques. The Examiner could have just as easily selected any two others of a multitude of scientific publications that teach standard transformation techniques and vectors such as these. Regardless, a person of ordinary skill in this field would not have modified *Famelaer's* method with a prior transformation step. Plainly, absent any exogenous DNA present, there would be no reason to select for chromosome fragments that contain exogenous nucleic acid and which exhibit normal plant chromosomal activities. Thus, in my opinion, my claimed invention would not have been obvious on the basis of these three scientific publications.

6. I declare under penalty of perjury that the foregoing is true and correct.

Dated: May 11, 2006

VICTOR KLIMYUK, Ph.D.

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